

## NIH LIBRARY TRANSLATION

### **NIH-98-134: Contemporary Medicine as Presented by its Practitioners Themselves, Leipzig, 1923:217-250**

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**Translated by Ted Crump**

If today, as a person approaching his seventies, I look back at the course of my scientific development, at the end result of my life's work, I can say with complete justification that what I have achieved I owe for the most part to those influences as a result of which the ability to make decisions was placed in my own hands. With all clarity I was able to discover in myself that the workings so readily invoked to clarify one's fate have no validity at all. Everything happened the way it had to happen. A long series of personal and material influences that were exerted on me since my childhood and generally followed each other in a purposeful way finally brought about that which I can count as the total gain from my scientific work.

I was born August 6, 1853, in Wesel in the Lower Rhine where my father worked as an assessor for the district court. My father's family originated from the Brandenburg March, while French blood flowed in my veins from my mother's side, inasmuch as her grandfather was forced to flee from France during the revolution and then later settled near Wesel. One of his sons, my maternal grandfather, was an attorney in Wesel. My father's father was an officer, and almost all my other family members of the male sex were likewise officers. Therefore, in my case one could certainly not speak of a hereditary predisposition toward medicine. However, there is an exception, insofar as the grandfather of my mother, Dr. Amedick, who also studied at Duisburg University, likewise practiced medicine in Wesel. But I never knew him. In 1856 my father came as an attorney to Duisburg, and in this city I spent my entire adolescence until my university years.

The Duisburg gymnasium was widely known for its strict discipline and the thorough manner with which the humanities were drummed into the pupils' heads. I still have the benefit of this. It seems to me as if we learned much more then; in any event, I read far more classics than is the case today. In addition to this intensive teaching of the classical languages, however, there was also instruction in the natural sciences, as they actually existed at the time. In any event, only two hours

per week were set aside for teaching natural sciences. However, I must immediately note, as a student I had never heard of zoology or botany, nevertheless in the first examination in medicine I passed in both subjects with a mark of one. For this I can only thank the men who taught me as a gymnasium student. In the lower classes it was H. Meigen; beginning with the third, W. Kohnen, who on the basis of very manageable teaching material taught us to see all things and look beyond them. It was also of no small influence that the extensive industry, the large number of chemical plants, the blast furnace facilities with all their accessories constantly had the effect of attracting the eyes and thoughts of the children unwillingly and unknowingly to the most diverse things and questions, the answering of which in any event could be reserved for more mature years. Thanks to the generosity of the Duisburg merchants and industrialists, apart from the rich zoologic collection, the gymnasium also possessed an equally well-equipped mineralogic and geognostic collection. In addition, a complete herbarium of the Duisburg phanerogamous flora was available from the estate of a deceased teacher. We were given an opportunity to examine this material thoroughly, always linked to the practical applications that applied at the time. Here my teachers proceeded without any pedantry. The result was that I, like most of my schoolmates, in my free time avidly collected what seemed to me worth collecting at the time, and at the conclusion of my gymnasium time had assembled a fair-sized herbarium as well as a collection of beetles and butterflies and a respectable number of minerals and fossils. The broad flood plain of the Rhine and the Ruhr, miles-wide forests and extensive meadow at that time made up the bountiful hunting grounds for these efforts. And from our teachers we could find out any information that we did not know and were keen to know.

The physical apparatus that was available to the gymnasium was very excellent, at least for that time. The Duisburg merchants and industrialists had also seen to it that later, when I heard lectures in Heidelberg from the physicist Kirchhoff, I hardly saw any experiment that was new to me. A magnificent battery of Grove elements and a large Ruhmkorff induction apparatus were in place in order to demonstrate to us the astonishing phenomena on the then still very new Geissler tubes. A large spectroscopic instrument, a good microscope, and much else were available for the use of our teachers and served for our education. On the free Wednesday afternoons, as ninth-year pupils under Kohnens direction, we became familiar with the elements of measurement science, learned to work with angle head and alidade and finally, as the highest achievement, to work with sextants and the theodolite.

Perhaps I have ranged somewhat afar in the description of these things. But I have had the conscious intent thereby to show how, despite good and thorough instruction in the classic sciences, notwithstanding expedient division of the time and with suitable faculty in natural science teaching, much more can be achieved than is usually assumed. In my lectures on pharmacology I often found it pitiful to find out with occasional questions what a miserable state the knowledge of my listeners finds itself in the simplest of natural science questions, despite the fact that they *lege artis* not only had been prepared for the first medical examination, but also

as their presence at my lecture proved beyond a doubt, had also passed it. Beyond this, from my school years I still think about the fact that the Duisburg Intermediate School had a small chemical laboratory, in which there were two hours of practical work on Wednesdays and Saturdays. I received special permission to participate in this work. It was still the good old days when a rubber stopper was a rarity, and we had to learn how to cut acid-fast stoppers from soapstone. I tried to acquire the necessary theoretical science through book study. This also had its great difficulties, inasmuch as specifically at that time the newer views, especially the type theory, had come to the forefront in chemistry, and I now saw myself always wedged between the aging formulas in my books and the new theory. But there I nevertheless learned that which one can certainly regard as small laboratory operation, and what one must expect as prerequisites in manual dexterity and knowledge from a proper laboratory worker. I would then meet with the professor of chemistry, Hoffmann, on Sunday evenings at the office of a pharmacist whom we both knew well, and who had a good microscope in his possession, and together with whom we examined all the marvels and wonders of nature.

Thus, in time I accumulated all kinds of natural science information in my skull. However, everything first came into actual use from my association with the man who certainly was of the greatest influence for my entire further development (even though he himself perhaps did not realize it) and with whom I have kept up a written correspondence: the general practitioner Dr. Ernst Weber. He possessed a very thorough and, above all, a very general knowledge. I learned much from him. In any event, our conversation avoided medical subjects. It much rather related to general questions, which interested him and myself. But he had such a way of getting to the bottom of things that may have shone on me somewhat. In any event he came to it on a foundation that had already been somewhat prepared. During our walks or on other occasions, my Grandfather Schulz had the not always pleasant way of answering my childish questions of why something or other was so first by answering, "Think for yourself why that is so!" and only then offering assistance.

During the War of 1870/71 I was first on vacation in Duisburg, then worked as a nurse in a military hospital in Wesel, and there experienced the first amputation and likewise the first autopsy on the cadaver of a French prisoner of war who had been shot in an attack on a guard.

In autumn 1872, I enrolled at Heidelberg University. Here it was above all the anatomist Friedrich Arnold who enthralled me. Together with Nuhn he directed the autopsy theater; both men were very attentive to careful and clean work. I will never forget the moment when Arnold said during a staff meeting, "Gentlemen, what you have not seen, should not exist for you!" With that he certainly did not wish to plant the seed of a cheap skepticism in the hearts of his listeners. We should rather learn to see with our own eyes and accustom ourselves to relying first of all on our own knowledge and our own work, and not take everything we read in the books at face value, and whose justification our own work was capable of clarifying.

Apart from Kirchoff, whom I have already mentioned, the two chemists Delffs and Borntrager were of particular influence on me. Delffs lectured on inorganic chemistry for physicians. It seemed more useful to me to attend his lectures than to attend the large presentations of Bunsen along with a few hundred listeners from all parts of the country. It was just our six who attended Delffs's lectures. But this had the advantage that the presentation took on a more personal character from the fact that the relationship between teacher and pupils was direct. In the summer semester, every afternoon from 2:00 to 5:00 there was a practical course in the chemistry laboratory taught by Borntrager. Thus there was enough time to familiarize oneself properly with inorganic analytic chemistry. This practical course also had a unique feature that later became an advantage for me. Borntrager administered the material to be analyzed in very low doses. One therefore had to learn from the beginning to make do with less.

In the autumn of 1873, I moved to Bonn and remained there initially until I had passed the State Examination. Of my professors in Bonn during my clinical period it was specifically the surgeon Busch and the internist Ruhle, as well as the psychiatrist Dittmar, from whom I gained the most. Later, when I was already a lecturer, Ruhle once entrusted me to take his place in the internal clinic during the autumn vacation. Of the theoreticians, it was Binz during my clinical period who introduced me to the basics of the specialization that was later to become my life's work.

But in my entire study time in Bonn and also beyond that, the physiologist Pflueger was of fundamental importance. From the first examination in medicine to the State Examination, I was like family with Pflueger. Under his direction I presented my first scientific paper at the Bonn Institute of Physiology: "The dependency between metabolism and body temperature in the amphibians." It appeared in Volume 14 of *Pflueger's Archiv* in 1877. In this work I was able to show that the metabolism of frogs was directly related to their temperature. Moreover, during the same period I also prepared another paper: "The oxidation of fats." This paper, which also appeared in *Pflueger's Archiv*, led me to the view that with the usual temperature, the oxygen of the air by itself is incapable of setting the oxidation of a fat into motion, even with sharply diminished partial oxygen pressure, but rather for oxidation the presence of one or more enzymes was required, which acted on the fat during their own degradation, or through their simple presence. We would say today, as catalysts, which first give oxygen the capability of oxidation.

During the university vacation in my clinical semester, I also had the particular luck that on a daily basis I could see and learn as much as I wanted to at the bedsides of the Vinzenz Hospital in Duisburg under the direction of the Medical Director, Dr. Otto Lange. It will be readily understood that particularly a city such as Duisburg, with its great industry, must have delivered everything possible by way of surgical and internal diseases to the hospital. Schiffer, who had come from Holland, also saw to it that I acquired a thorough knowledge of smallpox. In the afternoon I worked with my old friend, the pharmacist, and there acquired a fair knowledge of large and small operations in a pharmacy as they were undertaken at the time.

After finishing with my State Examination, following an old special interest I worked in comparative anatomy for another semester with Leydig. Then I went for one year to a polytechnic in Karlsruhe in order to broaden and deepen my knowledge of chemistry. During the Karlsruhe period, I applied myself to the solution of a question that I had encountered in my study of organic chemistry, especially organic arsenic compounds. In the manuals of the time it was always stated that cacodylic acid is conspicuously not toxic. With the aid of a preparation synthesized by my friend Wilhelm Lacoste, which had previously been tested for its identity with all rules of science, I was able to furnish the proof that animals intoxicated subcutaneously with cacodylic acid died with the signs of arsenic poisoning and also that these same signs of arsenic poisoning were present in the subsequent autopsy. Following this work, I then examined some phenylarsinic acids with the same result. These were likewise freshly synthesized by Lacoste, who at the same time together with August Michaelis worked on the topic in the laboratory of the polytechnic. Only later, when searching in the university library in Bonn, did I find the dissertation of Lebahn from the year 1868, which until then had remained completely unknown, and in which he had already presented a demonstration of the toxicity of cacodylic acid, and thus I was able to save for him the right of priority in the literature of chemistry and toxicology.

In the autumn of 1878, I became an assistant to Binz, in the Bonn Institute of Pharmacology, and in the spring of 1879 qualified for teaching in pharmacology based on the previously mentioned work. Together with Binz, and at his urging, I then carried out a long series of studies whose end purpose was to show that in the presence of living organic material of plant or animal origin the arsenious acid can be oxidized to arsenic acid. Despite numerous objections, we nevertheless succeeded in showing that our finding was justified. Apart from some smaller works, during my instructor time in Bonn I was also able to complete two other larger works. The first concerned eucalyptus oil. Its results were published in 1881 as a monograph.

At that time surgery was preoccupied with antiseptic wound treatment, and in the Bonn Surgical Clinic carbolic acid was intensively used. The unavoidable occurrences of intoxications, even cases of death, prompted the then Director of the Surgical Clinic, Busch, to turn to Binz with the request to recommend a non-toxic antiseptic for wound treatment. As far as I can now remember, at that time Thiersch had still not come out with his salicyl dressing. Binz, who himself had undertaken very instructive experiments on the efficiency of salicylic acid, did not place very much trust in it. He instead recommended eucalyptus oil to Busch, which had become known at that time, and he entrusted me with developing this topic. To put it succinctly, eucalyptus oil proved to be unsatisfactory for the purposes of the Surgical Clinic. Its irritating effect on the skin, of which I had long convinced myself with self-experimentation, made its use imprudent in the course of larger surgical procedures. Lister, who had likewise used the oil for a long time and had reported to me about it, also later abandoned its use.

The foreign literature, however, apart from its anti-putrescence and anti-fermentation properties, also reported on its conspicuous performance in malaria.

The objection that it contained toxic zymol had been raised against the internal use of the eucalyptus oil, and therefore its internal use was advised against. At that time I took the position which I have since relentlessly maintained: Whoever wishes to introduce a new pharmaceutical naturally must assume all possible guarantees for its effect on the human body! If zymol was actually contained in the essential oil from the leaves of eucalyptus, then it should be demonstrable because of the cuminic acid in the urine after its uptake. After I had become proficient in the demonstration of cuminic acid in the urine of animals poisoned with zymol at the Bonn Institute of Chemistry with the friendly assistance of Anschütz, I myself initially ingested 20 drops of pure oil every morning before breakfast for one month. I could never find cuminic acid in my urine. Its demonstration was even completely negative after I had taken an entire spoonful of eucalyptus oil in one swallow on two occasions. The applicable result of this self-experiment was that I could be completely reassured about the absence of zymol, and further had the opportunity to determine a number of phenomena on myself, which indeed did not belong to the category of absolute conveniences, but which gave me complete justification in stating that no foreseeable hazard for the life and health of the patient should be feared in the internal therapeutic use of eucalyptus oil. Later, in the treatment of tuberculosis patients, who could not rest because of their tortuous coughing at night, it never failed to render its service, sometimes with quite striking results. Why eucalyptus oil has not become accepted in medical practice has remained a mystery to me. Its extensive similarity to quinine in its behavior toward the spleen and the clinically determined fact, albeit thus far only abroad, of its good effect in malaria, especially where quinine has failed, nevertheless make it seem remarkable that we use the oil in malaria and otherwise do not and have not used it. Perhaps someone has feared an undesirable competition with the quinine preparations.

My second, larger work concerned the question of whether it is possible to break down chlorine compounds of alkalis and alkaline earths with carbon dioxide so that free hydrochloric acid should thereby appear. The answer to this question seemed both of balneologic and physiologic interest. The result that was unearthed came out positive, despite the difficulties that still existed at that time in obtaining a suitable method for the demonstration of this process.

The first year of my residency period also included, which may be of some interest, my concurrent work as a resident in the Hertz Mental Hospital, for which in any event only my free time was involved. Thereby I also learned much that I would not wish to be without today. Since at the same time I had also taken on the preparation of some articles for *Eulenburgs Realenzyklopadie*, I could not complain of a lack of activity.

My lectures as a private lecturer at that time concerned the chapter from pharmacology that could justifiably be termed elements, or in the manner of speaking of the material medica, as adjuvants, officinal plants and officinal, chemical preparations. I also lectured on the history of medicine and in the last semester about mineral spring and bath theory.

At Christmas 1882 I received my installation as full professor of pharmacology at Greifswald University. There began for me the time of the most far-reaching responsibility as teacher and scientist. In the middle of January I came to Greifswald, and the first thing I experienced was a great disappointment.

As a private lecturer I had paid little or no attention to conditions and circumstances in Greifswald. No one had ever expected Albert Eulenburg to give up his position of his own free will after nine years as Professor of Pharmacology. It had even less come into my mind that for me, as a young private lecturer, there were any prospects or hopes of becoming Eulenburg's successor. But things transpired as they were meant to, and one fine day I became a full professor. When I arrived here in Greifswald, to which I have remained loyal to this day, I found instead of the expected institute actually nothing. With the best of will, it was not possible to bestow the respected title of Institute of Pharmacology on a single room of the Institute of Pathology, which had one window, two gas burners, but no water, and in which everything was accommodated that belonged to the most minimal subsistence and necessities of a pharmacologist. There was not even a usable scale present. It will be understandable if everyone pitied me in the first days of my existence as professor in Greifswald. The preparations intended for demonstration in lectures had been placed for the greatest part in all manner of cartons, matchboxes, and bags, as well as in glass vessels of the most diverse type. It was absolutely enough to drive one to despair. But since nothing sensible has ever come out of such a mental attitude, I strived to do what could be done, since my pleas to the university curators at first remained totally unsuccessful.

In this period of my existence here there fall two observations that I had occasion to make and which, as I can positively say, were decisive for my entire future scientific activity and direction.

Since it could be foreseen that experiments on fermentation and putrescence in an institute of pathology would offer particularly good prospects for vigorous growth, I occupied myself as well as possible, in accordance with the state of our knowledge at the time, with this area. Sometimes, when working with substances that needed to be examined for their effectiveness in comparison to the inducers of yeast fermentation, initially working together with my assistant, Gottfried Hoffmann, I found in formic acid and also in other substances the marvelous occurrence that if I got below their indifference point, i.e., if, for example, I worked with less formic acid than was required in order to halt the appearance of its anti-fermentive property, that all at once the carbon dioxide production became distinctly higher than in the controls processed without the formic acid addition. I first thought, as is obvious, that there had been some kind of experimental or observation error. But the appearance of the overproduction continually repeated itself under the same conditions. First I did not know how to deal with it, and in any event at that time still did not realize that I had experimentally proved the first theorem of Arndt's fundamental law of biology.

While this observation after its publication had not received any particular attention, which certainly should not have been expected otherwise, a second observation was to affect my future more profoundly and become a guidepost for me. A practicing physician had published his findings in the use of extensively diluted veratrine solution in salmonellosis. I encountered this report in *Medizinische Zentralzeitung* of 1884. It interested me all the more, inasmuch as I had found in the literature that already at the end of the 1750s tincture of veratrum lobelianum had been used for the same purpose in Silesia and reportedly had been a success. To tell the truth, at that time I knew nothing about the properties of veratrine beyond that fact that it could be irritating to the skin and also its well-known influence on the process of contraction in the frog muscle. Thereby, however, there was not much to start with in the present cases and for any kind of explanation for the very conspicuous effect of veratrine in salmonellosis. But perhaps an explanation could still be obtained if a third property of the alkaloid was enlisted. Its qualification as an extremely intensive "protoplasmic toxin," as people used to say, was well known. The bacilli required to induce salmonellosis had just been discovered, and on this basis the entire utility of veratrine therapy in salmonellosis was explained as simply as possible: The parasites found in the intestine were rendered inactive by the effect of the veratrine, and thereby the disease came to an end. My colleague, Paul Grawitz, at my suggestion declared himself immediately prepared to explore the matter in more detail experimentally. In my so-called institute I could not even think of carrying out such experiments. At that time an institute of hygiene still did not exist in Greifswald. Therefore the cultures of the microorganisms responsible for the salmonellosis were acquired. I prepared the nutrient media with varying veratrine content, Grawitz assumed the inoculation and further cultivation in the Institute of Pathology, and then something completely unexpected occurred: Despite an addition of veratrine, which went far beyond all measure—the highest concentration in the nutrient medium went up to 0.1 percent—the sowed cultures grew, which was a real surprise. The veratrine was taken from an absolutely certain source. Why didn't it work, and why did the colleague from the practice have good results?

At that time, upon further consideration, I began to have the first misgivings about the widespread and universal interpretation of the so-called antiseptics and protoplasmic toxins as direct bacillus-killers in internal therapy, a consideration that in later years at one point again flashed like a meteor in the therapy heavens as the great sterilization therapy. When I also objected that a veratrine intoxication in humans can have an eerie similarity to an attack of salmonellosis, and that a high-degree enteritis could be found in animals intoxicated with veratrine, then an assumption of compelling necessity arose: If the veratrine treatment actually helps, and there was not doubt of this from the findings in medical practice, then it can only come about in such a way that under its influence some kind of change appears in the diseased stomach and intestinal wall, which creates unfavorable conditions for the further development of the microorganisms and the sequelae resulting from this. It was the first thought about the profound importance of the diseased organ



as the nutrient medium for the disease-causing factors and the resultant, not less profound importance of organ therapy in its totality, not only for the therapy of infectious diseases alone, as in the present case. This viewpoint obtained at the time was subsequently further intensified and reinforced. It became central for me throughout the entire period of my scientific activity. It created for me the necessary inner justification, both in my subsequent publications and also with respect to my pupils, to continually examine the close relation between drug effect and the diseased organ and the consequences that result with compelling necessity for drug therapy.

The publication of my finding, together with the theoretical remarks pertaining to it, continued to lead to nothing for therapy. Just as little as a few years later, my reference to the excellent results obtained by Aulde in Philadelphia with other colleagues in his practice with the use of copper arsenite in very low doses in Asiatic cholera. Even then I had become suspicious of my colleagues with respect to the unusually low doses at which the veratrine as well as the copper arsenite had worked. It smelled very much like homeopathy! However, after I sent him my veratrine work, my friend Ernst Weber wrote me, "Now you will have the hounds after you!" He was right. Since the publishing of this work I have not only had the homeopathic lay organizations on my heels. Even some of my specialist colleagues have used this and my subsequent work to assist me in acquiring the honorary title of the "Greifswald homeopath."

Since, as a result of the unfavorable conditions in the institute at that time, I had much time at my disposal, I used it to increase and deepen my knowledge of the history of medicine. Thereby I particularly focused on the area which encompasses medical sectarianism and heresy. Thus I became more familiar with Paracelsus, as well as with the old Rademacher and the father of homeopathy, Hahnemann.

In the inner processing of the new things that I learned in my historical studies, I became convinced that it always signifies a loss for drug therapy if one simply passes over with disdain the experience of physicians who have gone their own way in the use of medicines. The fact that, with their methods of administering drug therapy they had indisputable successes in certain areas, cannot be dismissed so simply and with a mere gesture.

At that time I initially did not go any farther in my train of thought. The future first necessitated that I devote the necessary light and achieve clarity. My treatment of the oldest natural history that we possess in the German language, the *Book of Nature* of Konrad von Megenberg from the beginning of the fourteenth century, should be regarded as the result of further historical studies in the area of general natural sciences. I translated his text into New High German and commented on its content, but I would hardly have been able to do either if I had not had a language and natural science background from my gymnasium instruction.

After much letter writing and oral appearances before the pertinent authorities, finally in the autumn of 1886 I was able to have space in the old building on Domstrasse, whose use had previously been harmoniously shared by an obstetric clinic

and the Institute of Chemistry, allocated for my institute. Now I could finally think of at least somewhat orderly work, and no longer had to use the pipe from the tiled stove in my private residence as an incubator, and could transfer the analytical scale that I had obtained in the meantime to more worthy housing in the new institute.

From this time on, my work in the scientific area more clearly divided into two parts than it had previously. One corresponded to purely experimental work, the other to the theoretical considerations and conclusions that followed therefrom. I will first discuss the experimental work.

Prompted by study of Hahnemann and his followers, I decided to pursue the basis of the matter further and to experiment whether actually through continued intake of small amounts of pharmaceutical that one would regard as intrinsically ineffective, pathologic manifestations could be induced in healthy human subjects of the type described in Hahnemann's drug tests. I was given much kind assistance in these studies on the part of my assistants and students.

I need not especially emphasize that in these experiments on healthy human subjects all possible and conceivable caution was expended in order to avoid errors and delusions from the beginning. Apart from myself, of course, none of the persons involved ever knew what they took. For those studies in which I had several participants available, at least for one, for the most part for several, I would run blind studies as well, i.e., these subjects received only pure water or pure alcohol, depending on the type of substance tested, and were obliged to present their case history just as well as the others did. I also repeatedly discussed the entire manner of these experiments as well as their end purpose, even if there was no further success as was to be expected, in my publications, e.g., in a special article in the *Deutsche Medizinische Wochenschrift*.

Apart from everything else, in these drug tests on healthy human subjects, another special circumstance was important for me. Even as a student and then repeatedly at a later time I had often enough experienced that the various animal species under certain circumstances can behave quite differently and sometimes totally differently from how humans behave if they were under the effect of one and the same substance. In any event this was nothing new, just as the likewise frequent enough observation that, for example, in frogs of the same species just the time of year and internal as well as external conditions under which the experimental animals directly found themselves could influence the result of studies of intrusive substances in a quite remarkable way. To this was added the further consideration that one actually had to deal first of all with the influences of pharmaceuticals on the human body, and finally the fact that it could be easily shown mathematically that quite little active substance was involved in the effect of the mineral water used as a medication, if one calculates it according to the quantities that tend to be taken of such mineral water daily for therapeutic purposes.

A large part of the results of my pharmaceutical experiments is included in dissertations. Of my own I wish only to mention the experiments with iron, quinine, and sulfur as well as those carried out with silicic acid. They showed, in order to establish this first of all, that the data I had found in the pharmaceutical studies of

the homeopathic school were correct. In any event, we were not able, apart from a few exceptions, to learn the effect of the substance to the finest detail as Hahnemann, for example, had described. But this is certainly based in part on the fact that my experimental material was made up of young, strong, and healthy persons, who were accustomed to the use of alcohol and tobacco, and above all had no time to pay attention to all possible changes in their condition. I exercised particular caution in the experiments with sulfur, in that I only announced their results after I had repeated the first experiments after an interval of 10 years, naturally with entirely different individuals and, I would add, also with the variants that in one series I had the subject ingest the sulfur in a powder with lactose, and in the second experimental series in an alcoholic solution. Naturally, the result in both cases, and despite the different conditions, was the same.

The fact that these experiments also must have provided useful material to those of my colleagues, who sensed the more or less developed need to present the Griefswald pharmacologist as a dreadful heretic and thereby discredit once and for all as a scientific worker, I knew beforehand, and it did not concern me further. My purpose was to obtain the truth, and let the result come out as it may. So then, unfortunately, I squandered an entire semester testing Jager's data of his so-called neural analysis. In brief, these experiments were carried out in the university building in a room given to me for that purpose in order to rule out all unavoidable external influences in an institute from the air impregnated with chemicals and animal exhalations. At that time I worked with table salt, which I had purified by means of repeat recrystallization and precipitation with alcohol. Likewise I also prepared the dilutions myself with observation of all rules of caution. Neither my assistant, Dr. Mittelstaedt, nor I myself could know in each individual experiment whether we were working with pure alcohol or with some kind of table salt dilution. The flasks that contained the various dilutions or pure alcohol were always transferred to us by the institute suppliers without labels and a special accounting had to be kept of their withdrawal. Thus every personal suggestion for my assistants and me was ruled out. The end of the story was, as we were able to determine, that everything only came down to practice. Finally, with every table salt solution we could reduce our personal equation to zero or almost zero equally well as with pure alcohol.

Following the experiments on the effect of sulfur and silicic acid on the healthy human body, I then undertook a long series of other types of studies. For sulfur I wished to establish its level in human and animal organs in the expectation that I would be able to find a simpler analytic method that could contribute to clarification of the question. To what extent I was successful in this, also with respect to the manner of determining the total urinary sulfur within a short time, without the burdensome evaporation and subsequent destruction of the remaining residue, I will leave to the decision of those who have their own more extensive experience in the area of work.

In my studies of silicic acid I first made the surprising discovery of what a significant role it plays in the makeup of connective tissue and then especially how much its quantitative occurrence in connective tissue is dependent on this stage of

development. I then found strikingly high values for the acid in the embryonic connective tissue of Wharton's jellyfish, values which approached the silicic acid content of salpas and holothurians. It was necessary to put this finding down as erroneous on the basis of an analytic examination. Thereby I was forced to go through the entire boring work once more. Its numerical result came out exactly the same as in my first analysis. It is always burdensome, and harmful for the future development of one scientific question or another, if people whose analytic skill, because of the nature of the business, does not allow for any particularly high demands, on the basis of their work feel justified in exercising disparaging criticism on the work of other. Nevertheless, it is such a daily occurrence that it is not worth speaking about it further.

The expectation I had once harbored, and which I assumed to be supported by considerations of geologic conditions, that silicic acid could play a role in the genesis of goiter, was not supported on the basis of numerous silicic acid assays in goiter of North German and Swiss origin as well as longer dietary studies in rats. On the other hand I was able to show on the basis of over seventy individual assays that the statement that appeared in 1914 to the effect that the pancreas had a particular inner relationship to silicic acid metabolism in the human body, and that the silicic acid content of this gland is below the norm in tuberculosis and above the norm in carcinoma, is untenable. In the material which my colleague Grawitz kindly supplied, rather irregularly I would one time find a conspicuously high level in the pancreas of a person who had died of tuberculosis, and conversely strikingly little silicic acid in the salivary gland of a person who died of carcinoma.

Here I would like to add to this, and especially stress my viewpoint, that after interest in silicic acid had once been aroused by my work, soon thereafter several comments appeared in our scientific literature, which with respect to the therapeutic applicability of the acid made all manner of suggestions, especially in consideration of its use in pulmonary tuberculosis. On that I have the following to say: Actually and above all at the present time we do not have any experience in the therapeutic benefit of silicic acid. Certainly, however, sufficient material can be found on this question in the homeopathic literature. This school has already worked for a century with silicic acid if one would be also of advantage as well as desirable and beneficial for the patients to be treated with silicic acid if one would for the time being accept the findings made there. One would save much time and many disappointments.

The studies of chronic ozone intoxication, fluorine compounds, and the effect of phosphorus hydride, all carried out on animals, also fall in the first period of my experimental activity. Since in the course of the years I had become completely accustomed to being viewed as an unworthy in the working area of pharmacology, and likewise had become accustomed to not stirring any interest among my specialist colleagues with my publications, I decided, in order to best fulfill all demands, to undertake a work in which the result of animal experiments, experiments on healthy human subjects, and finally the collected data as well should be found, which in the bedside use of the substance about to be named was collected and had been

published in the literature. I published the result of this work in 1914 in a monograph under the title: *The treatment of diphtheria with mercuric cyanide*. Whoever among my readers has further interest in this matter will wish to read this monograph. Thereby, however, one should not be shocked by the fact that in our serum-free time nothing further has been pursued about it, and not because this time as well one of my colleagues disparagingly criticized my work in such a way that I was amazed that I still had any students signing up for my lectures on pharmacology.

My last work came at the end of the wartime period and in its direct sequelae. In one case it showed me the possibility that quinine can periodically induce yeast fermentation. This work cost an endless amount of pain and vexation. Each individual experiment had to be carried out over several days. For that purpose a complicated apparatus was required, which was dependent on electric power and gas. As an expression of the strike that was so much in favor at the time, these two factors tended to fail with a type of demonic punctuality precisely when the answer to the questions that interested me was knocking on the door. Now I can't repeat them again.

This is because by far the greatest part of the second group of my experimental work was carried out in the present-day, new Institute of Pharmacology. In 1908, I was given the former Institute of Chemistry and was finally, after approximately 25 years, placed in a position to work as I would have liked to from the beginning. It will seem quite impossible to many of my readers to learn that in the old institute in the Domstrasse in the first years, the water that was required for the laboratory work had to be obtained by the bucketful from a supplier until the erection of the municipal water supply also eliminated this calamity.

The second group of my experimental works exclusively encompassed studies of whether the biologic principle stated by Rudolf Arndt would actually stand up to demonstration of its correctness or not. If his first theorem, that weak stimuli promote the vital activity of organs and organisms, is correct, a toxin in sufficiently reduced quantity must no longer be harmful, but rather its influence should have a beneficial effect on the substrate. I have already said that at the beginning of my presence here I had the proof of this in my hands. The next concern was to find a method which satisfied two requirements: The product of the vital activity must be determinable according to a certain measure, and secondly for the supplier of this product every possibility must be ruled out of being disturbed by some kind of undesirable external or internal influences. Therefore, I decided to work with the aid of yeast and to implement its carbon dioxide production as a measure for the work performed. Today I can certainly assume that the result of this experiment is generally known. In any event, it elegantly proved the correctness of the first Arndt theorem. Later on it was also repeatedly confirmed by others, even with the use of other starting material. But, whoever takes into consideration what it means to have to carry out such experiments without any specialized assistance in the construction and preparation of the apparatus, that it was already a success if one or more of the apparatus did not fail because of bursting or leaking, and the process had to be

started all over again, will readily understand how I rejoiced when finally I found myself in possession of some actual utilizable, even numerically, final results.

Subsequently, I never took my eyes off the question of the possibility of experimentally proving the correctness of Arndt's law. The study of the natural science and medical literature continuously gave me new substantiation that it did in fact involve a natural law. However, I wanted to possess data which, by originating from my own work, would also provide me with absolute personal certainty. Thus I finally came upon the idea of selecting the human visual organ as a substrate for my studies. Since the results obtained in this way also again showed with all desirable certainty that Arndt's law in its first theorem, which, as I will show again at a later point, still had a quite particular meaning for me, is in fact correct. All experiments with their methods and final results were published in *Pfluegers Archiv* and can be consulted there. Apart from that, I also provided my pupils, Kurt Wienver and Hans Strubing, with additional material. The following substances were tested: santonin, gratiola, oleander, caffeine, and alcohol. The possibility of any suggestive effect on the result on the part of the observer was here also painstakingly avoided by the entire experimental arrangement. I must emphasize this point again, because I have had the experience that I was reproached for this possibility, and that this was used as a cheap basis and aid in casting doubt on the correctness of my work.

I now turn to description of the second part of my scientific activity, which operates in the purely theoretical realm. When in 1885 Rudolf Arndt for the first time expressed his views in detail as we were taking a walk together, and explained his basic law of biology, it was if a sudden illumination had come over me. A very large part of my work came directly out of it. Arndt, as I stated in the article "*Rudolf Arndt and the fundamental law of biology*," had no recognition among his contemporaries, and never found respect. Among other considerations that came to mind for me, I regarded it as my duty as friend and colleague to at least preserve his memory from complete oblivion. It need only be mentioned in passing that my article was rejected by several of our scientific publishing houses and so finally had to appear here in Greifswald as a monograph.

The views that I had formed about the essence of the actual drug effect, in which no longer influences on the healthy body of a human or animal species were involved, but rather the treatment of pathologically changed organs and organisms, naturally were not the product of limited time. I myself had to first completely re-learn them. I had to rid myself of many views that still were left over from my school years. Thus, for example, in my first publication from the year 1884, in which I dealt with the treatment of diphtheria with mercury preparations, I still based myself on the antiseptics prevailing at the time. I still believed in the possibility that after internal administration, the mercury excreted by the glands of the oral cavity could directly attack the pathogenic microorganisms. But already by 1885 I learned to regard as certain that every strong drug effect was based on the direct treatment of the actual basis of the disease, and that an actually effective influencing of infection-causing noxae by pharmaceuticals as it was conceived of at the time is absolutely impossible.

For apart from the infection pathogen, its carrier was placed under the influence of the pharmaceutical at the same time. Here I would like to add a recollection that has stayed with me and originated from my lectures from that period. I lectured about quinine, and thereby discussed Binz's findings of its harmful influence on protoplasmic structures, including the white blood corpuscles, and for my listeners I then developed, quite logically as I thought, how in malaria the quinine attacks the plasmodia and in a favorable case renders them entirely unviable. Then an alarming thought suddenly occurred to me that was not exactly advantageous for the flow of the presentation: If the quinine actually is a toxin for protoplasm, why after it has been ingested does it not attack the white blood cells, but rather limits its action to the pathogen of malaria? If the leukocytes are also involved, what results for their owner, what consequences are there for all life processes, if with one stroke the white blood cells are crippled and therewith at least for a time become incapable of working?

In the time to come I racked my brains very much over these and other considerations, all the more so since at that time nothing was known of the possibility of driving success in malaria therapy specifically with quinine because of its strong stimulation of phagocytosis. At least I did not know of it. This was joined by the very obvious consideration that drug therapy involves taking diseased organs into account. However, with respect to their behavior in a healthy state, these exhibit a quite different, essentially increased excitability by certain pharmaceutical influences, insofar as they can react to them at all. If the basic law of biology is correct, it results from its first theorem that one must be capable, with a sufficiently decreased dose of the correctly selected, organ-specific pharmaceutical, of bringing the declined vital energy up enough so that the physiologic norm is either entirely regained or regained to the greatest possible extent. It likewise follows from the same law that a dose selected too high by necessity must have a harmful effect because of overexcitation. In my first publications on this question, following on the cellular pathology established by Virchow, I still take the view that one should strive after a cellular therapy as much as possible. So, for example, in the article that appeared in the *Deutsche Medizinische Wochenschrift* in 1890 entitled "Task and goal of modern therapy." Later I came back from this view, essentially because I had to say to myself that we actually know very little, let alone anything useful, about the internal living conditions and life processes of a healthy cell, and further, that for the pharmaceutical therapist it is not the behavior of the cell, but rather that of the organ or the organism which in the final analysis is and must be decisive. However, it remains a fundamental requirement for any therapy constructed on this basis that in the individual disease case one is able to actually select the pharmaceutical that most and best responds to the disease picture present. The indispensably necessary knowledge of the drug effect in general and in particular will never be achieved if one wishes to construct his knowledge solely on animal experiments and some toxicologic findings in humans. It is not healthy animals, but diseased humans that make up the working field of the practicing physician. Further, however, occasional observations at the patient's bedside

alone cannot give an actually generally applicable material for correct assessment of a pharmaceutical. The influence of individuality also more or less makes itself known in each individual case in drug therapy. Here, naturally, I completely leave out of consideration the use of those substances which only satisfy the conditions that are involved for the moment. These have nothing to do with an actual organ therapy. If we can draw conclusions about the effect of a drug promising lasting results in its use at the bedside, we must know in advance on which organs it works, and how it is capable of changing the behavior of healthy humans.

This is not the place to treat and discuss all these questions individually and extensively. In my publications I have repeatedly treated this chapter, sometimes as the main subject. But it seems appropriate to me to discuss how I have shaped my teaching and lectures in accordance with my views. Before I go into detail on this, I would like to preface with an observation that is grounded on the facts and also must be comprehended and assessed in accordance with them. In the course of the years I was able to determine that my lectures increasingly enjoyed the interest of the attendees. The lecture time both in winter and summer was in the afternoon at 4 p.m. to 5 p.m. Admittedly, this time of the day is not exactly favorable. The students have spent the entire morning in the clinics. They are certainly no longer as fresh and receptive as in the morning. To this is added the high outside temperature in summer and the enticement to go out into the great outdoors and let the school dust blow out of their ears. Often enough I was astonished in the middle of summer when entering the auditorium to find good attendance despite the warm weather outside. Since I certainly could say of myself that I had never belonged to the feared examiners, the pleasing frequency of attendance could certainly not have been based on the grounds, always to be assumed by the student as possible, that one could present himself in the best possible light at the state examination by having good attendance with the examiner. So I certainly was not entirely wrong when in wondering why the students attended so persistently, including a theoretical course as well, I arrived at the assumption that they themselves must have the feeling that they could have some advantage from the lectures for their later activity as physicians. Up until the war I also gave a so-called practical course in therapy twice weekly at 8:00 to 9:00 a.m. This was by no means a required course. The practical course in therapy was intended only for later semesters. On the basis of an assumed disease case all possibilities of a therapeutic nature were discussed, which could be regarded as coming into consideration for the assumed case before us with all its variants. I also regarded it as my duty on this occasion to present to the young students of medical science the therapeutic measures and beyond this to teach them those that are to be regarded as lying outside the so-called school medicine. In addition, naturally also went a detailed examination of the nature and quality as well as the special mode of action of the individual pharmaceuticals. The course was given in the manner of a colloquium. A lively discussion often ensued. Whoever disagreed with any of my statements, had not understood something or wanted to know something, could freely express himself about it. I myself learned very much in all those years during which I held this lecture.



Apart from my students who belonged to this university, up until the outbreak of the war I repeatedly had foreign colleagues in the practical course in therapy, especially from Holland and Sweden, for the most part already fully trained physicians. It was always a particular satisfaction to me if occasionally I would learn by letter or by word of mouth that in the practicing of their profession my former students, who already long had their own practices, had been able to use what they had taken from the practical course in therapy with good success. Such reports always gave me new courage to continue the path that had already been laid down.

Since in the regular lectures on pharmacology with occasional questions from the audience unfortunately it repeatedly came to light how little natural science knowledge was developed in the great majority of listeners, I made an effort to prepare the Greifswald physicians in this area as extensively as possible. Within my power I wished to save them the embarrassment for later that in the occasional conversation in the tavern the pastor or the schoolmaster proves to be better informed about one poison plant or another or whatever should grow out of the forest floor than the doctor. In more recent years I have often enough to my inner aggravation had the experience that even the district medical officer, as he was still called at that time, had no idea about things that he rightly should have been able to learn in school, in any event later at the university. In the summer I also repeatedly made botanical excursions with them at the request of some of my students. On such occasions the gentlemen were quite often astonished to find out by seeing themselves what actually grows in the outdoors by way of toxic and medicinal plants. In the winter when the inorganic pharmaceuticals were mainly worked with, I always showed my listeners, with material from a small mineralogic collection of the institute, what the raw material looks like from which the inorganic pharmaceuticals were made. But here or in any other occasion I never went into detail in the chemical formulas. From abundant experience I know precisely that the majority of the physicians tend not to think about this very much or at all, and because of the examination would only burden their memory with all manner of formulas and reactions which later in their practices would serve them no purpose.

Finally, let us consider yet another particular point. In my lectures I never demonstrated animal experiments. In my view these belong to the laboratory. I could never see the value, say, of the demonstration that one can anesthetize a rabbit with chloroform as a teaching aid. But I always said to my listeners that they should take advantage of every opportunity in the clinic and there observe how a human behaves during and after anesthesia. Experiments with animals linked to larger procedures not only takes away time unnecessarily, but apart from that, strictly speaking, they have only toxicologic interest or are already known to the students from their lectures on physiology. I also know full well from my own student days that such experiments for the most part have more the value of stunts for the audience and are a welcome break from the spoken lecture, than they can be regarded as teaching aids properly speaking.

As a teacher I always had only one purpose in mind, and was always in pursuit of the one goal of offering as much to my students for their future position as physicians and for life as I could and knew. There was nothing for which I was not ready at all times to take full responsibility.

It is a long-known fact that, particularly in the area of drug therapy, the most diverse tendencies and directions have developed since the earliest times. The history of medicine proves this on every page. From the crudest priest and folk medicine to the methods of developing and applying pharmaceuticals equipped with all the aids of the most modern research, from the earliest times there have been the most diverse variants and viewpoints. Some of them came about as quickly as they disappeared. Others have endured through centuries of the human race, often enough despised by the contemporaries of their founder, banned, and then finally recognized as justified. I believe the future physician should be schooled to some extent in these things. If only to create for him a freer view of the area in which he will deal every day in his later position as physician: drug therapy. If in the course of a lecture I had the opportunity to speak about how and on what basis one pharmaceutical or another is deemed practical by another school, I always made an effort to present the scientific possibility for such an assessment as clearly as possible. For that purpose it was naturally necessary to go into more detail in the historical development and discuss the external conditions and circumstances, under which they developed. At the end of such a discussion I always said to my listeners, "What I have presented to you, I place at your completely free disposal. You can do with it what you like. You should come to a binding conclusion from your own considerations and act accordingly thereafter. I teach no dogmatism!"

On the other hand, if there was sufficient opportunity, I never neglected to give my audience a chance to freely discuss with me what I thought about our present-day drug therapy and the path that pharmacology had taken as a curriculum subject. Today this has become almost entirely the monopoly of the chemical industry. It brings its new preparations onto the market, but how many of the physicians who prescribe them to their patients have anything more than a mediocre idea of what they are prescribing? Quite apart from the substantiation of the medical value of all the new substances through experiments on healthy animals, perhaps also on animals artificially made ill, and also not always entirely unobjectionable, later follow-up tests with healthy humans. Every practicing physician will confirm for me that over the long term there is no real relying on all these new preparations, despite sometimes glowing advertising, and they are forced sooner or later to turn to something else. For the chemical industry this naturally can only be proper. It is first of all concerned with the money that can be made with one new product or another. If it no longer moves, as the businessman's expression goes, something new is thrown on the market. In the end effect the dividends are what is important, a view that is completely justified for the industry, but not one to be recommended for medicine!

In my lectures to the students as well as occasionally in my publications, I have often spoken on this topic. I have talked with colleagues and pharmacists about this.

The actual result naturally at first remained negative. Quite frankly expressed, it was a matter of pure business concerns. Therapy provides only the flag under which the boat sails. Trust in the old, proven medicines, except for a few remnants, has completely disappeared. The new medicines owe their possibility to exist essentially to the clever advertisements with which they are offered to physicians and patients. As a renowned representative of the profession of pharmacology and in the knowledge that one bears and should bear the responsibility to his listeners of what one should recommend to them for their future medical activity, what should one say when chemical factories publish thick books in which not only their preparations are shown, which would be understandable, but also served up together with indication and dosage with all accessories in such a manner that one actually needs to hear or know any pharmacology teaching. The name of the disease is listed in the registry, the page number leads to the naturally much-tested and proved pharmaceutical. One only needs to write down the additional information that is given and shove the prescription into the patient's hand. Everything else will work out! Strictly speaking, this is the point of view of the famous shepherd, Thomas, can also practice quackery. First and foremost it relieves the therapist of any independent thinking, which for many may have its pleasant side. And since the human body, even in pathologic states, is for the most part much more resistant than one usually tends to assume, such drug therapy in most cases is not accompanied by further harm to the patient. In other cases, this is by no means so. The unconsidered use and uncritically continued application, sometimes over long periods of time, of a preparation from the chemical industry, can subsequently lead to consequences that must of necessity and according to the very simple laws of nature harm the patients. Actually what has been said thus far is self-evident. It has often enough been admitted to me in occasional conversations with colleagues. But with the regretful shrugging of the shoulders: "What can one do? The substance is recommended by this or that person, who should know, and the public demands it, therefore how should one proceed in practice?"

Drug therapy is in a severe and for the moment quite hopeless struggle: business versus science! I will certainly readily admit that among all the new drugs this one or that one may serve its purpose, assuming that it is used under careful establishment of the indication and in correspondence to the greatest extent to the individual case. But in how many cases is there enough time to provide this condition of the necessary usable observation material, which again is self-evident? For the most part it is unforeseen, so-called side effects which set in, often other factors as well, which lead to such a substance disappearing from the market and another brought on the market in its place with the necessary promotion. I posed for myself the question again and again: How can a physician take responsibility for working with drugs about whose type and composition he perhaps knows nothing, and, in view of the way that the substances tend to be researched, at the most and in the best case scenario can only know individual details about their actual effect on the human body?

On more question in conclusion: What does pharmacology in its present form offer the physician? Pharmacology, as is known, evolved from the old material medica. It sought to create order in the tangled mass of therapeutic details of all manner of myths and uselessness which in the course of time had accumulated. The development which the entire medical science has taken since the middle of the last century has not failed in its inestimable influence in this direction as well. First of all, pharmacology combines the most essential part of its task and work toward determining the reasons why a pharmaceutical works one way and not another. Therefore, through the work in the pharmacologic institutes we have achieved an insight into actual conditions, very much contradicting previous assumptions which corresponded to the overall point of view of science at the time, but could not go much beyond conjectures. Knowledge took the place of speculation. With it, so to speak, the individual drugs were in hand quite differently from before. To this was then added a whole series of new discoveries and findings, which naturally had to be adjusted to the further development of the study of the drug effect. The then highly pertinent questions regarding substances which appeared to be suitable for providing a satisfactory effect in the area of antiseptics, effective and reliable antipyretics, and then, as the era of somnifacients set in, the search for such agents that could combine sufficient effectiveness with the required safety—all these questions were extensively developed by pharmacology, apart from many others, many of which could lay claim to more extensive interest on the part of the clinicians. But that which should have been expected from the beginning: a closer relationship between the clinic and pharmacology, a more intensive use of pharmaceuticals at the patient's bedside based on pharmacologic research, has not developed. I have become acquainted with clinicians who directly oppose the results of pharmacologic institutes, insofar as they are directly linked to drug therapy. The reason for this certainly very undesirable phenomenon lies in the fact that the conclusions drawn from experimental results on animals, even healthy ones, when applied to diseased humans and their behavior under the same drug effects, often enough proved to be erroneous, and, strictly speaking, had to be proven erroneous.

The fact that pharmacology takes all possible forms of life as working objects, from infusoria and leukocytes to mammals, gradually led to its becoming a type of comparative toxicology. In any event, the clinic could not and cannot do anything with it. In its further development pharmacology then became more and more of an appendix to physiology. It essentially works with the methods of the latter; the animal experiment has become the decisive thing. I was once told by a younger, more energetic colleague that the effectiveness of a pharmaceutical is only actually scientifically present and can be regarded as substantiated if the animal experiment has spoken its last decisive word. Then, in accordance with the developmental path of this colleague, I may assume that he is not the only person who holds this view, and that he thereby did not just express his own thoughts.

To be brief, today the immense quantity of all kinds of effective and ineffective substances which the old material medica still dragged along with it has been

replaced by a not much smaller quantity of experimental studies. Frankly, their results have not brought the benefit to the clinic that one certainly might have expected. Here, naturally, I am excluding the abundance of hypnotics, antipyretics, remedies for nervous diseases, tonics, and other things. As I have already pointed out, in the end they all serve only to combat a single symptom and have little enough to do with the actual disease, from which they always seek to eliminate only a certain sequela or secondary condition. The further consequence, however, has been that, despite all work in the pharmacologic laboratories and working chambers, the knowledge of the special pharmaceutic effect in individual detail has increasingly disappeared. I have often enough heard it in my life, both from students as well as especially from physicians, that they actually have never understood what all the marvelous information on the influence of certain substances on the frog and dog esophagus, the frog heart, the organs of rabbits, guinea pigs, dogs, and cats in general, was supposed to teach them. In practice they could not do much with what they had learned. Our present-day clinicians, however, have also attended these same pharmacology lectures at one time and had to assimilate its experience. The consequence of this must naturally have been that for their part they became less and less able to offer their listeners what was still taught in the clinics fifty years ago and on which the practical activity of the earlier physicians in the field of drug therapy had rested. Or have all only erred throughout their entire long lives? Following contemporary views and modes of speech, has their science, which in everything else is exact, only shown random successes in the area of drug therapy? Let's be quite frank: What actual real value, for example, has the vast sum of experimental work on digitalis shown for the treatment of heart diseases? Hecatombs of frogs have been treated with it, the most diverse theories have been posited of how the digitalis effect should effect the frog heart. Has anything in particular changed as a result in its use at the patient's bedside? Perhaps the external form of its use could have become more expedient, thanks to the help of chemical technology. But this is all. On the other hand, a large number of agents long known to be effective and usable at the bedside have today been completely forgotten. To adequately explain their mode of action with certainty just with the aid of animal experiments alone would not succeed. Thereby they have become lost for medical practice. Where should the student learn about them? But the suffering humanity bears the damage from this. What help is a theory of the effect of one drug or another artificially constructed with all aids of the most modern research and viewpoints, if in practice it either totally fails or in the last analysis only provides confirmation of what has already been known in practice for a long time? The great danger lying therein is that theoretical research will be given preference over practical experience, indeed dismissing the latter as quite meaningless, has been recognized by insightful physicians for centuries. I need only recall the words of Paracelsus, a man who stands as great as a physician as he does a thinker, that the theory should emerge from practice, not the other way around! If experience shows and has shown that a certain pharmaceutical is itself effective in a certain area, it should not then simply be thrown into the storeroom, because the

theoretical consideration and research fail with respect to the ultimate mode of its action.

If students and physicians are actually to derive a benefit from pharmacology, they must pursue other ways than they have chosen thus far. They must not regard the animal experiment, which in and of itself certainly cannot be completely dispensed with, as the last criterion for the value or lack of value of a pharmaceutical. Their main task should be to find the value of the individual pharmaceuticals for the practice from the overabundant data offered by the old and new literature, to present the result to the young learning physicians and to stimulate these to use what has been presented to them at the patient's bedside. It is all self-understood, without any kind of damage and impairment to work in the laboratory, whose area is indeed so endlessly vast. In this manner pharmacology will become a useful and actually utilizable aid to the clinician. One cannot expect him to devote his time to researching older and newer pharmaceutical literature only for the purpose of informing himself more thoroughly on the use of a particular drug. A not insignificant part of the activity of the pharmacologist comes into play here. Its result must be for the benefit of the clinician and thereby also for the general practitioner.

Herewith I have offered my readers the briefly summarized result of work and thought processes which look back over a period of forty years. The study and teaching of pharmacology has been my life purpose. If I had to start over again today from the beginning, I would take the same path without further consideration and continue to follow it, even though seen from the outside this path thus far may have shown little visible success. A single clinician has thus far regarded it as important enough to explore the path that I have taken alone for long years on the basis of Arndt's fundamental law of biology in the recognition of its fundamental importance for therapy: the Berlin surgeon August Bier. Thereby the first breach is laid in the wall of disregard and in places even direct distortion of what I wanted. Perhaps in the changes of time sooner or later an internist will take a closer interest in my work, which has only had the purpose of serving medical science and thereby also, insofar as possible, medical practice, regardless of whether it enjoyed the approval and understanding of renowned and unrenowned critics or not.

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